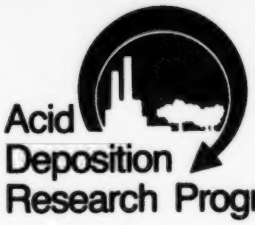

FINAL REPORT

OF THE

SCIENCE ADVISORY BOARD

TO THE

MEDICAL DIAGNOSTIC REVIEW PROGRAM

JULY 1986

Acid Deposition Research Program

This report represents the Final Report of the Science Advisory Board on the Medical Diagnostic Review study for the Acid Deposition Research Program.

As noted in the preamble of the enclosed report, the Science Advisory Board to the MDR was appointed immediately following the Banff workshop held in January, 1984, in response to recommendations from participants in that planning session.

The SAB was thereafter involved in the development of the Request for Proposals (RFP) for the MDR, in the selection of the best proposal submitted and, indeed, proposed several modifications to the proposal, all of which were met by the Principal Investigator. In July 1985 the SAB members made a site visit to the Hill Spring facility and reviewed and approved the physical arrangements, procedures and progress to that date by the medical research team.

A penultimate copy of the MDR Report was reviewed by the SAB on May 30 to June 1, 1986 and recommended changes were incorporated into the MDR Report released to the public on June 11, 1986. It was arranged at that time that a final, subsequent review meeting would be held so that the MDR-SAB would be able to present its review comments on the exact copy released to the public. Due to print deadlines and the timing of the public release this could not have been accomplished earlier. In any case, the comments noted earlier had been dealt with in the Final Report of the MDR.

The final SAB meeting was held on July 15-16, 1986 and this report is the result of that meeting. Dr. Hill was unable, due to international travel commitments, to attend that meeting in person, but his concurrence with the review report was obtained by telephone.

The SAB is, therefore, an essential part of the MDR study. It constitutes the key peer-review aspect of the study by a body of internationally respected medical and health science professionals. Having followed exactly the protocol earlier established, this SAB process completes the final, review aspects for the MDR established by the Acid Deposition Research Program.

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FINAL REPORT

of the

SCIENCE ADVISORY BOARD

to the

MEDICAL DIAGNOSTIC REVIEW PROGRAM

July, 1986

July 16, 1986

The following review of the Report on the Southwest Alberta Medical Diagnostic Review Project represents the consensus opinion of the Scientific Advisory Board (SAB). The SAB was asked to review the Report by the Members Committee of the Acid Deposition Research Program (ADRP) of Alberta, Canada.

I. Background:

A. Early activities of the Scientific Advisory Board (SAB):

The SAB was appointed following the workshop held in Banff on January 22-27, 1984. Participants in the workshop had recommended the creation of a Scientific Advisory Board composed of appropriate experts from outside of the Province of Alberta. The workshop participants also recommended that a medical diagnostic review be undertaken in the region subsequently designated as the Index Area (IA).

The original SAB members included Drs. B. Burrows (Chairman) from the University of Arizona, Z. Annau from Johns Hopkins University, W. Mertz of the U.S. Department of Agriculture, J. Samet from the University of New Mexico, and M. Utell from the University of Rochester. Dr. Burrows visited the Twin Butte area on June 3-4, 1984 and made an initial contact with concerned residents of the area. On July 11-14, 1984, the entire SAB convened for the first

time, visited the area of concern, had an open meeting with the public and heard Dr. Earle Snider present his views on the health problem. At this meeting, the SAB concluded that in order to evaluate the health status of residents of the area, a major Medical Diagnostic Review (MDR) should be undertaken. This recommendation was in accord with the conclusions of the Banff workshop. The region of primary concern (the IA) was specified by the SAB on the basis of long standing reports of excess symptoms and illness in the area, reported excess heavy metal burdens in residents of the region, and general proximity to an operating sour gas plant which was considered by many residents to be the cause of their health problems.

To implement the program, it was decided to develop a Request for Proposals (RFP). Guidelines for preparation of an appropriate RFP were provided by the SAB to Dr. R. Rogers of Alberta, who was then the manager of the project. The draft of the RFP was reviewed and modified by the SAB through the mail and with subsequent conference calls.

Following its approval by the SAB, the RFP was widely distributed in Canada. Dr. W. Spitzer of McGill University in Montreal submitted the only proposal which responded adequately to the requirements of the RFP. The SAB reconvened in Atlanta on March 15-17, 1985 to review this proposal in detail. (Dr. Samet was unable to attend this meeting; however, he transmitted his review of the proposal to Dr. Burrows prior to the meeting.)

B. Atlanta Meeting (March 15-17, 1985) of the SAB:

In addition to the SAB, this meeting was attended by Drs. Rogers and Stokes from Alberta as well as by Drs. Spitzer, Steinmetz, Schechter, and a representative of Eco-Technitrol Laboratory. While approving the general outline of the proposal, the SAB requested several modifications prior to its implementation. These included:

1. The selection of comparison communities should be reconsidered. One should be in the vicinity of a sour gas plant.

2. The determination of certain heavy metals and selenium in biological samples, including hair, should be carried out concurrently with the diagnostic evaluation.

3. The investigators should identify and utilize a reliable laboratory for hair analyses with assurance of quality control. Dr. Mertz would assist in selection of the laboratory and was delegated to act for the SAB in approving final selection of the laboratory to be used.

4. Environmental monitoring should be deleted from the MDR program. (The SAB considered that special monitoring would not be relevant to the goals of the MDR which was not designed to describe exposure-response relationships.)

5. The questionnaires should be modified to make them more appropriate for this specific project.

In addition to recommending specific modifications of the proposal, it was agreed that the SAB should reconvene in Calgary to perform a site visit as soon as possible once the first phases of the project had been completed. Dr. Spitzer was requested to submit a revised final proposal incorporating the above recommendations with a revised budget. The latter would take into account any additional expenses incurred by these modifications.

The SAB was kept apprised of the implementation of Phase I of the MDR by Dr. Rogers and subsequently received, by mail, a copy of the final proposal in early July 1985. During the interim, an appropriate laboratory was selected for trace element analysis after site visits by personnel from Dr. Mertz's laboratory. The laboratory selected met with Dr. Mertz's approval.

C. The July 13-14, 1985 meeting of the SAB in Southern Alberta:

The following summarizes the SAB's impression of the status of the Medical Diagnostic Review in July 1985.

The SAB met on July 13 and 14 in Alberta, made a site visit to the Hill Spring facility and reviewed the physical arrangements,

procedures, and progress to date with Dr. Spitzer and his colleagues.

It was the opinion of the SAB that the Medical Diagnostic Review had been successfully implemented. The SAB were quite impressed with the achievement of establishing such a large facility at a site so remote from Montreal. The measurement procedures, including physical examination, questionnaires, blood and urine tests, spirometry, and electrocardiograms, were satisfactory. Dr. Mertz planned to follow-up on certain aspects of the collection of the hair samples. Plans for the studies of cancer incidence and mortality outcomes were described and considered satisfactory. The investigators had adopted an innovative plan for identifying outmigrants. The specific methodology for evaluating the occurrence of birth defects had not yet been developed.

Dr. Spitzer requested approval to add 300 additional subjects in the Stirling-Raymond area. This expansion was to permit a stronger comparison between findings in this sample and the population in the DCCI area. Because of the low cost of adding these subjects in relationship to the potential gain in information, the SAB supported this request. It was specifically stated, however, that a comparison of results in the DCCI and Stirling-Raymond areas should not be construed as an epidemiological assessment of the health effects of any environmental pollutants.

In summary, the SAB approved the Medical Diagnostic Review. Dr. Spitzer had implemented a program that was technically sound and, with the exception of agreed upon modifications, should meet the goals of the original Request for Proposals.

D. Subsequent Activities of the SAB and its Chicago meetings (May 30 to June 1, and July 15-16, 1986):

In December of 1985, Dr. Gerry Hill of the Alberta Cancer Board was appointed to the SAB to assist in evaluation of the final Report of the MDR.

A complete draft of the Report was delivered to each member of the SAB on May 22, 1986. All SAB members then met in Chicago on May 30, 1986 for a preliminary meeting to exchange their views. On May 31, they met with Dr. Spitzer and several other members of the team involved in the MDR to discuss the draft report. As a result of this meeting, some minor revisions in the Report were made. A later draft of the results and conclusions sections of the Report was delivered to members of the SAB on June 3, 1986. A definitive review was not possible prior to public release of the Report on June 11.

Dr. Burrows attended the meeting in Pincher Creek on June 11, 1986 at which the Report was made public. A subsequent meeting of the SAB, which had been planned previously, was held in Chicago on July 15-16, 1986. At this meeting, the following Review of the

Report was formulated. Dr. Hill was not able to attend the July 15-16 meeting, but his concurrence with the Review was obtained by telephone.

II. Review of the Report:

A. Methodology

The Southwest Alberta Medical Diagnostic Review Project (MDR) was carried out to determine if there was an excess burden of disease in the Hill Spring/Twin Butte/Glenwood/Willow Creek/Mountain View Region (Index Area). A variety of adverse health effects had been implicated by area residents and some previous studies. As stated in the RFP,

> "Residents in the study area have been complaining for several years about health problems ranging from dire consequences (e.g. cancer, increased mortality, adverse pregnancy outcomes, etc.) to less serious chronic problems such as increased allergies, skin rashes, sore throats, headaches, lethargy, eye irritation, respiratory tract infections, etc. Domestic animals have also been reported to be affected to varying degrees."

Thus, the mandate in the RFP issued by the ADRP was broad; a comprehensive medical survey was required to address the current

health status of the area residents, the mortality in the Index Area, cancer incidence, pregnancy outcomes, birth defects, and the possibility of trace metal toxicity of Index Area residents. The MDR provides information on each of these health outcomes. Each of the component projects is reviewed separately below.

Selection of appropriate comparison areas was critical for testing the investigation's principal hypotheses. The McGill team recognized the importance of proper comparison area selection and approached this task with a rigorous method. Census tracts were compared on relevant characteristics with a multivariate approach. This technique provided satisfactory justification for the choice of the Stirling-Raymond (SR) Area as the "Unexposed Most Similar Control Area". Selection of an "exposed", and demographically comparable area was found to be impossible. Instead, an area (called the DCCI in the Report) was chosen as one "exposed" and representative of all provincial census tracts.

The limitations of the concept of "exposure", as used in this report, must be recognized. By design, in the context of this investigation, "exposure" refers to residence in an area with a sour gas plant. In accord with recommendations of the SAB, the dimensions of this "exposure" designation were not further characterized by detailed air quality monitoring or other environmental data.

The component studies included a cross-sectional survey and retrospective cohort studies of cancer incidence and of all-cause mortality. The validity of these studies depended strongly on describing patterns of migration out of the Index Area and comparison areas, and evaluating cancer incidence, mortality and health status of outmigrants. The investigators recognized this problem and extensively evaluated the experience of outmigrants from the Index Area. While the investigators could not contact all of the outmigrants from the Index Area, the results of the survey are reassuring. Given the difficulty of tracking outmigrants, a remarkably high number were contacted, and it was learned that health was an infrequent reason for leaving.

The cross-sectional design that was used for the central component of the project represented a straight-forward application of conventional epidemiologic methodology. The investigators achieved the needed high response rates of greater than 90%, and important bias from the small number of nonparticipants is unlikely. Given the range of potential health effects and the more general concerns about ill health in the Index Area, the investigator's decision to provide a comprehensive medical evaluation was appropriate. The SAB concurs with the use of a standardized health history, a ritualized and conventional clinical assessment, and the selected laboratory examinations. The methodology for the retrospective cohort study of the 1970 cohort members is also appropriate.

The SAB commends the McGill investigators for instituting numerous quality control procedures in the setting of an exceptionally large investigation conducted on a stringent timetable. Their efforts provide assurance that random and non-random errors have been minimized. In addition, the SAB commends the investigators for utilizing a Scientific Advisory Group of distinguished biostatisticians, environmental health scientists, and epidemiologists as independent consultants to the study.

The data analyses and presentation are largely descriptive. Statistical significance levels were not specified and adjustments for confounding factors were not performed in the analyses presented in the Report. The SAB concurs with the general analytic approach. In the Index Area, virtually the entire population participated; thus, sampling was not a source of variability in this group. The multiple comparisons made in examining the large number of data items further complicates interpretation of significance levels. The Report also provides satisfactory justification for not routinely adjusting for potential confounding factors.

The investigation has specific and intentional limitations, which are acknowledged in Section III below.

B. Review of Morbidity Studies:

The current health status of the IA was examined by conducting a cross-sectional study. The following end-points were examined:

Current physical disability
Utilization of health services
Chronic illness
Symptoms
Clinical findings
Laboratory studies
Lung function studies
Clinical diagnoses

Considering the large number of health end-points studied, the SAB was impressed that few showed substantial or possibly meaningful differences between the IA and comparison areas. In fact, none met the stringent a priori criteria for clinical significance established by the investigative team.

The SAB agrees with the conclusion that there was no detectable increase in physical disabilities as assessed by activity loss for the residents of the IA compared to comparison areas. Additional findings indicate that health services and medications were not more frequently utilized in the IA than comparison areas. No

differences in the prevalences of common chronic diseases (including diabetes, epilepsy, heart disease and kidney disease) for the communities were detectable.

In an attempt to examine a large array of biochemical markers of injury, routine laboratory studies were performed on blood and urine. There was no difference in the percentage of participants from the different communities with biochemical abnormalities. Similarly, electrocardiograms revealed comparable frequencies of rhythm and conduction disturbances in the communities, and lung function was remarkably similar in all areas. Thus, these objective tests revealed no excess abnormalities in the IA.

Information on symptom and illness rates were obtained through diverse data collection techniques including: questionnaires on symptoms (including those during the two weeks before examination) and on the cumulative prevalences of selected illnesses between 1970 and the examination; a standardized physical examination; and, in selected instances, an evaluation by a consulting physician. The results were provided separately for symptoms, the ritualized examination, and the diagnoses reached by the judgmental and consulting physicians. For some illnesses, the symptoms and/or examination results were combined to create new illness categories.

For the symptoms during the previous two weeks, the questionnaire responses showed a general pattern of higher prevalence rates in

the Index Area. The findings were similar in children and adults, and extended across all organ systems. These results document the increased symptom rates that had been described previously and in part motivated this study.

The general pattern for the period prevalence of reported illnesses, 1970-1985, was comparable to that for symptoms. While none of the differences between the Index and comparison areas reached 10 percent, the SAB noted that "reported hypertension" (18.7% vs 11.2%) and "chronic bronchitis or phlegm lasting more than one year" (16.4% vs 10.8%) were more frequent in the Index Area.

Despite an excess of symptoms and reported illnesses in the IA, findings on the ritualistic examination failed to reveal an excess of abnormalities in the Index Area. This was especially noteworthy in regard to the eye examinations and measured blood pressures. Indeed, certain findings, such as "red eyes" and "red mucosa" were found much less often in the IA than in Stirling-Raymond. Also, the reported excess in symptoms suggesting chronic bronchitis was not accompanied by an excess of findings indicative of that disease, either on physical examination or lung function testing. The interpretation of the excess reported rates of symptoms in the IA is discussed further in Section III.

With regard to the clinical diagnoses reached by the judgmental and consulting physicians, the prevalences of the most common

illness diagnoses were low and similar in the Index and comparison areas.

C. Reproductive Risks and Outcomes

The design of this component of the study is a cross-sectional comparison of the three areas based on the reproductive histories of those women interviewed in 1985, plus the outmigrants who spent at least one year of child-bearing age in the area between 1957 and 1985. Data on fertility problems in males, on developmental milestones, and on the prevalence of birth defects in the children are also included. The design is weaker than a cohort study, but the latter was not feasible. Many of the data are derived by recall, and the results must, therefore, be interpreted with caution.

Data are presented on the following outcomes: age specific fertility rates, proportion of pregnancies leading to fetal loss (spontaneous abortion and stillbirth), proportion of low birth weights (less than 5 1/2 pounds), prevalence of birth defects as reported by mothers and found on examination, and the percentage of children with delayed development. These definitions are appropriate summaries of the available information.

The data suggest lower reported fertility rates and a higher incidence of reported fetal loss in the IA compared with the comparison area. The proportion of women reporting fertility

problems was slightly higher in the Index Area than the comparison area, but a similar differential was not seen for the exposed comparison area. A higher incidence of reported birth defects was also found in the IA compared with the comparison area, but this difference was not supported by the prevalence of birth defects found at examination. No differences were found with respect to birth weight or development.

The investigators conclude that the small differences which were observed are not clinically significant. Given the nature of the data this conclusion is reasonable.

D. Trace Metal Studies:

Human exposure to environmental chemicals can be detected by measuring the concentration of these chemicals in a variety of body fluids or tissues. Analytical techniques for measuring trace elements in hair samples have been developed to the point that this noninvasive method is frequently used as a first screen for detecting excessive exposures. The accuracy of this method varies for different chemicals and is critically dependent on the quality of the particular laboratory performing the tests. Paired with blood and urine determinations when necessary, hair analysis can be a useful diagnostic tool.

Numerous hair analyses have been performed on the residents of the Index Area in the past. The results of these analyses have not

been published, but have greatly alarmed those residents who were told of potential contamination by metals. It is the opinion of the SAB that the validity of these measurements is in doubt, because no information regarding the strict quality controls essential for obtaining accurate results was available. Because of these privately released hair sample measurements, some residents undertook chelation therapy or, in the event of alleged trace element deficiencies, trace element supplementation.

Given the deeply felt concerns of the residents over this issue, the SAB recommended that hair analyses of certain metals and trace elements be undertaken during the MDR. In addition, it was agreed that blood or urine samples would also be available in order to provide additional (and often biologically more relevant) material for verification of excessive burdens.

The potentially toxic metals chosen for study included mercury, lead, arsenic and cadmium, because of their known toxicities. The trace element chosen was selenium because of the concern that the soil of the areas may be selenium deficient. Other elements such as iron, chromium, aluminum, copper, calcium, and zinc were not included, because at the present time the relationship between hair levels for these elements and alterations of biological function in a healthy population are not established. This is discussed further in Section III.

The dominating concern in the choice of laboratories and procedures was with quality control, given the difficulties of trace element analysis. The main performing laboratory was selected after site visits of independent experts in trace metal analysis. Accuracy was ascertained by inclusion of the only available certified reference hair material (from the Japanese National Institute for Environmental Studies). Ten percent of the samples were also analyzed by the Trace Analysis Laboratory of the Mayo Clinic. That protocol assured a maximal degree of accuracy, given the present state of the art.

The methods of collection - mild shampooing, stainless steel scissors, stapling to a cardboard, no vigorous chemical cleaning of the samples in the laboratories, may possibly have introduced some metal contamination of minor importance, but if it occurred, it would have exaggerated the indications of heavy metal exposure.

The accuracy and precision of both laboratories was excellent for cadmium. Both were slightly low, but within the acceptable range of error for selenium. For lead and mercury, the principal laboratory was at or close to the certified values, with the Mayo Clinic Laboratory significantly lower. The trace metal concentrations used in the Report are from the principal laboratory, which is documented to be highly reliable.

The results, expressed as median and percentile values, clearly show no differences in hair levels of heavy metals between the IA

and the comparison areas; if anything, the Index Area values may be lower for some elements. A few hair samples showed heavy metal concentrations outside of the accepted normal ranges; further analyses on blood or urine of these individuals were performed. In the few cases where high blood or urine levels confirmed the hair data, the subjects were notified and referred to a physician.

Relatively high selenium concentrations were found in the hair of approximately 100 individuals, and in 25% of these cases also in the blood. These levels are not considered to be a health hazard; they may be associated with the use of selenium supplements or selenium containing anti-dandruff shampoos.

With regard to the adequacy of environmental selenium, 8.3% of the individuals sampled in the Index Area had "undetectable" hair selenium levels compared with 4.9% in the SR and 3.1% in the DCCI areas. As discussed further in Section III, this suggests a lower selenium status in the Index Area as compared to the comparison regions, a question not adequately addressed in the Report.

The SAB agree with the conclusion that the hair analyses were well controlled and showed no evidence of higher exposure of the population in the Index Area than in the comparison areas to Hg, As, Cd, or Pb.

E. Cancer and Mortality Components:

The design of these components is that of an historical cohort study. This is appropriate for delayed events leading relatively quickly to death, so that a prevalence study is out of the question. Membership in the cohort is defined by residence in the Index Area at any time during the calendar year 1970. This is a reasonable approach, particularly in regard to determination of cancer mortality.

The historical cohort was identified by a combination of methods including various administrative records and intensive local inquiries. This process appears to have been carried out assiduously and due account has been taken of the reliability of the information. It seems highly improbable that any loss involved could bias the results.

The two outcomes are registration with malignant neoplasm (ICD 140-208) by the Alberta Cancer Registry and registration of death by the Alberta Vital Statistics Division. Both registers are based on permanent residence at time of diagnosis or death respectively. It is acknowledged that cancer registrations or deaths occurring out of province are not included. Some such events occurring elsewhere in Canada would be transferred back under inter-provincial arrangements if their permanent residence was in Alberta. This would not occur for temporary residents in the United States or for permanent residents outside Alberta. The

person-years at risk in the cohort has been calculated for residence within Alberta to make these denominators comparable with the numerators and with the comparison rates. This is clearly appropriate.

The restriction of critical cancer events to all malignant neoplasms, and all except non-melanotic skin cancer, is appropriate.

The reference areas chosen to calculate expected events are entirely appropriate. In any case, it is clear that the results are much the same for all comparison groups.

The statistical methods used are standard for analysis of cohort studies. The power calculations establish that important differences are unlikely to have been missed.

The conclusion that the cancer incidence of mortality from all causes experienced by the IA is in keeping with what would be expected based on appropriate reference groups is, in our view, entirely justified. The above average incidence of skin cancer in the south of Alberta is well known and, as mentioned in the Report, is easily explicable in terms of sunlight exposure.

F. Conclusions of the Report:

The SAB concurs with the overall thrust of the conclusions of the Report on the MDR. Clearly, there is no evidence of increased mortality, of an excessive overall rate of cancer, of increased exposure to toxic metals, or of an increased prevalence of serious disabling disease in the IA. The findings of the MDR should provide residents of the Index Area with assurance that their general health status is good. Also, there is no distinctive pattern of clinical findings suggestive of a disease syndrome peculiar to that region.

The SAB also agrees with the overall conclusion of the Report concerning less serious health problems, but has additional comments concerning symptom prevalences and some other findings in the MDR. These are discussed below.

G. Recommendations of the Report:

The SAB concurs with the recommendations of the investigators in the MDR but has additional remarks which are presented below in Sections III and IV.

III. Comments of the SAB:

A. Scope of the MDR:

At the time of the drafting the Request for Proposals for an MDR, the SAB recognized that any study of the Index Area would have certain inherent limitations and that no feasible study would be likely to satisfy all residents of the area who had health concerns. The major objective of the MDR was to determine whether the longstanding complaints of residents of the IA reflected a clinically important health problem in the area. The MDR was also designed to determine if there was a special pattern of adverse health effects in the region which would suggest a specific environmental health problem. The data in the MDR provide unequivocal answers to these questions. No evidence of a clinically important health problem was found, and no pattern of adverse health effects suggesting a specific environmental health problem was detected.

Specific limitations of the MDR include:

1. The MDR was not designed to detect temporal fluctuations in symptoms or other health outcomes in relationship to any type of environmental exposure. Such a study would have been fraught with difficulties, both in regard to measurements of exposures and in regard to determination of health end points. Individual exposures vary greatly

even within a small geographic area and are dependent not only on emission sources and meteorologic conditions, but on a variety of other factors such as time spent outdoors and local irritants and allergens in and around both the home and work environment. Particularly during inclement weather, individual exposures may be much more dependent on the indoor than the outdoor environment, and the two may differ markedly both quantitatively and qualitatively.

Studies of temporal effects are even more difficult when there are no clear hypotheses regarding the specific substance(s) suspected of having an adverse health effect. Without such an hypothesis and without a distinctive pattern of suspected adverse health effects, it is impossible to determine a priori which health end points should be examined. If a distinctive pattern of adverse health effects had emerged from the MDR, and particularly if these had suggested excessive exposure to some particular type of noxious agent, there would have been a rationale for suggesting a study of possible short term health effects related to changes in environmental pollution. Since this was not found, the SAB concludes that a study of short term changes in health status in relationship to the environment cannot be justified in the Index Area.

2. The hair analyses in the MDR included those elements which are known to be toxic in levels that could occur as a consequence of environmental exposure. While it is possible to measure a wide variety of other substances in hair, they were not studied for one or more of the following reasons: a. the relationship between their hair concentration and human health is unknown; b. there are no generally recognized limits of normal for the substances; or c. the measurements themselves are of questionable reliability.

   For example, it is well known that large quantities of iron salts, far more than could occur from environmental exposures, may be ingested with impunity. Indeed, iron supplementation is often taken to insure an adequate store of body iron for synthesis of hemoglobin. Human diseases in which there is an excess body burden of iron are secondary to inborn errors of metabolism or congenital abnormalities in hemoglobin synthesis. Acute iron intoxication only occurs in children who ingest very large quantities of iron supplements. Aluminum poisoning has only been observed following prolonged renal dialysis. In neither case has analysis of hair been accepted as the medical procedure of choice for diagnosis of intoxication.

It is beyond the scope of this review to discuss separately all of the metals which have been perceived as a problem in the Index Area as a consequence of previous hair analyses. These were performed without adequate quality control and interpreted without regard for the state of knowledge about the potential toxicities of the substances involved. The SAB is convinced by the evidence in the MDR that there is no environmentally induced problem with heavy metal toxicity in the Index Area.

3. The possibility of a relative deficiency of selenium in the soil of the IA was recognized by the SAB, and the higher proportion of undetectable selenium levels in the hair of residents of the IA tends to support this concern. However, the hair analyses performed in the MDR did not allow quantification of hair selenium levels of less than 0.1 ppm. Thus, the presence of a higher frequency of undetectable selenium levels does not necessarily indicate a true selenium deficiency in any residents of the study areas. Indeed, the only known deficiency disease related to selenium (Keshan disease) is endemic only in China and occurs only under extreme conditions of very low environmental selenium, low protein intake, and near complete dependence on locally grown foods. The lack of characteristic clinical findings in the MDR virtually excludes the possibility that Keshan disease is endemic in the IA. Furthermore, the

infrequency of undetectable hair selenium levels in the DCCI speaks strongly against exposure to sour gas plant emissions as the cause of low hair selenium levels in the IA.

Because it has been shown that in some areas of southern Alberta there is a low selenium content in the soil, the low hair selenium levels measured in the MDR are a cause for some concern. The biological significance of these measurements could be established by evaluation of health data already obtained in the MDR. If symptoms or clinical findings are related to low hair selenium levels, further studies would be indicated, including glutathione peroxidase measurements in red blood cells to confirm the presence of a low selenium status.

4. The MDR was not designed to be a study of the health effects of any specific source of pollution. While it is reassuring that serious adverse effects were not found in the areas exposed to emissions from sour gas plants, this does not prove that such emissions may not induce discomfort in certain sensitive individuals.

B. Cancer Incidence Data:

As noted previously, the data in the MDR provide unequivocal evidence that the areas studied do not have an overall incidence

of cancer which is higher than expected. In fact, the incidence of lung cancer is remarkably low and speaks strongly against the possibility of an airborne carcinogenic agent in the IA. However, there is a tendency toward a high rate of prostate cancer. An above average incidence of prostate cancer in the southeast portion of Alberta has been reported. The fact that this could extend to the southwest is interesting. Case control studies of skin and prostate cancers in Alberta have been completed, and the results are being analyzed. These may shed further light on the factors related to these diseases.

C. Prevalence of Symptoms:

As acknowledged in the Report, a variety of symptoms are reported in excess in the Index Area. In some cases, the symptoms reported are difficult to associate with the environment, as with the prevalence of hip and leg discomfort. There are, however, consistently high rates of symptoms relating to the eyes, nose, and lower respiratory tract that could result from exposure to an airborne irritant or allergen.

It is reassuring that these symptoms are not associated with physical signs indicative of a chronic or serious disorder of these organ systems. The low rate of respiratory cancer provides strong evidence that any airborne irritant which might be present is not carcinogenic, and the lack of lung function abnormalities indicates that there is no serious disease of the lower

respiratory tract. Nevertheless, the possibility that there is a mild environmental irritant or allergen in the IA which can induce discomfort in some residents of the area cannot be totally excluded.

The ocular, nasal, and respiratory symptoms of concern are completely nonspecific and could result from a wide variety of factors, ranging from high local levels of dust to a mild airborne chemical irritant or even an allergen from local vegetation. These symptoms are so common in many areas that the frequency with which they are reported is also dependent on the health consciousness of the population being studied. Regardless of their origin, however, the symptoms rates do indicate that more of the residents of the IA than of comparison areas are aware of the discomfort in the eyes, nose, and respiratory tract. The MDR provides assurance that these symptoms, while an annoyance, are not indicative of a serious underlying health problem. Since the scope of the MDR was remarkably comprehensive (actually exceeding the initial expectations of the SAB), the SAB agrees fully with the investigators in the MDR that no additional study would allow more definitive statements to be made concerning the subjective complaints of residents of the IA.

D. Variability in Rates of Disease within the Index Area:

Inevitably, there will be those who criticize the MDR for failing to compare rates of symptoms and findings in different locales

within the Index Area. Even on its preliminary visits to the area, the SAB was impressed with the fact that the residents of certain regions were much more concerned about their health than those of nearby communities. In addition, apparent clusters of certain conditions (such as cancer and birth defects) were reported by residents of the area. However, since such clusters are likely to occur in any area solely as a result of chance, differences between relatively small population samples within the IA would be impossible to interpret. On the other hand, an environmental factor adversely affecting a large proportion of the residents of the IA would be expected to produce some increase in the rates of disease for the entire area. For these reasons, the original design of the MDR recommended by the SAB did not include within-area comparisons as part of the study but emphasized the need for a comprehensive evaluation of all residents of the IA.

IV. Recommendations of the SAB:

1. The SAB wishes to emphasize the first recommendation of the Report. None of the findings in the MDR should be used as a justification to relax efforts to control industrial emissions. The SAB also wishes to emphasize that the MDR was designed to assess the health status of residents in a specific geographic area. Its results should not be interpreted as a study of the potential impact of sour gas plant emissions on human health.

2. We concur fully with the second recommendation of the Report concerning the desirability of upgrading the registration of birth defects occurring in Alberta.

3. We also concur with the third recommendation of the Report concerning the inadvisability of new data collection concerning the health status of residents in the Index Area. The very comprehensive studies incorporated in the MDR should be regarded as the definitive examination of the health of residents in the region. However, the results of the MDR do not exclude the possible need for future studies of health effects of specific industrial pollutants in Alberta.

4. In order to determine if the naturally occurring low selenium levels in the IA might have any implications in terms of human health, limited additional analyses of data already available in the MDR should be carried out. It should be determined whether subjects with undetectable hair levels of selenium show an excess of adverse health effects which might be ascribable to a low selenium status. If this is found, additional studies of this specific question may be indicated.

5. The SAB recommends that if any new studies of health effects in Alberta are initiated, they be subject at all stages to rigorous peer review by recognized medical, toxicological, and epidemiological consultants.

V. Acknowledgements:

The SAB wishes to congratulate the investigators in the MDR for their ability to carry out a very comprehensive health survey under difficult circumstances. We also wish to commend the ADRP and the Government of Alberta for their willingness to support an inherently complex and expensive study in response to the health concerns in a relatively small area within the Province. We are impressed with the care that was taken to prevent any outside pressures from influencing either the conduct of the MDR or the process of its review. The invaluable assistance of Drs. Robert Rogers and Ron Wallace in the management of the study is also acknowledged. Finally, we wish to thank the community participants in all study areas for their cooperation and support of the MDR throughout all aspects of the study.

SCIENTIFIC ADVISORY BOARD MEMBERS

We concur with the July 16, 1986 Review of the Report on the Southwest Alberta Medical Diagnostic Review Project.

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* Dr. Hill was unable, due to international travel commitments, to attend that meeting in person, but his concurrence with the review report was obtained by telephone.